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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,030	08/12/2004	Norbert E. Fusenig	0471-0286PUS1	3120

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EXAMINER	
HENRY, MICHAEL C	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
08/06/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/501,030	FUSENIG ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,22-27 and 30-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18, 22-27 and 30-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/08/09 has been entered.

The following office action is a responsive to the Amendment filed, 07/08/09.

The amendment filed 07/08/09 affects the application, 10/501,030 as follows:

1. Claim 18 has been amended. Claim 19-21 have been canceled. New Claims 36-38 have been added. The rejections of the prior office action made under 35 U.S.C. 103(a) and mailed on 01/08/09 are maintained.
2. The responsive to applicants' amendments and arguments is contained herein below.

Claims 18, 22-27 and 30-38 are pending in the application

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 18, 22-27 and 30-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willoughby et al. (WO 94/23725) in view of Pressato et al. (WO 97/07833).

In claim 18 applicant claims "A method for the treatment and care of primary and secondary tumors by inhibiting angiogenesis which comprises applying at the tumor site a biomaterial comprised of a benzyl ester of hyaluronic acid wherein said hyaluronic acid is a total benzyl ester of hyaluronic acid, wherein said hyaluronic acid is 100% benzyl esterified and wherein said biomaterial inhibits angiogenic processes related to vascularization by granulation tissue forming over the biomaterial and wherein said biomaterial is in the form of at least one member selected from the group consisting of a non-woven felt, sponge, microsphere, film and membrane." Claims 22-27, 30 and 31 are drawn to said method wherein the hyaluronic acid is in association with other natural, synthetic and/or semisynthetic biopolymers, pharmacologically active substance, specific pharmacological active substance and specific form of application to tumor site and wherein the vascularisation and specific tumor cell invasion is specifically limited.

Willoughby et al. disclose the use of hyaluronic acid, including hyaluronic acid esters for the treatment of tumors by inhibiting or regressing angiogenesis (see claims 48-58; see also claims 24-34). Furthermore, Willoughby et al. disclose that their invention provides a process for the inhibition, control and/or regression of angiogenesis, (for example the inhibition of blood vessel growth to a malignant tumour, cutting off blood vessel growth or development, in to a malignant tumour) in a mammal (for example a human), the process comprising the steps of administering an effective dosage amount of a pharmaceutical composition for the inhibition, control and/or regression of

angiogenesis to a site on/in the mammal in need of inhibition, control and/or regression ….. (see page 7, lines 6-32; see also page 6, lines 13-21).

The difference between applicant's claimed method and the method disclosed by Willoughby et al. is that Willoughby et al. do not recite the use of a specific ester (i.e., benzyl ester) of hyaluronic acid but teach that esters of hyaluronic acid can be used.

Pressato et al. disclose a biomaterial comprised of benzyl ester of hyaluronic acid in the form of gels, membranes, woven tissues or meshes and nonwoven tissues that can be used to prevent surgical adhesion (page 5, lines 20-26). This suggests that benzyl ester of hyaluronic acid can be in the form of gels, membranes, woven tissues or meshes and nonwoven tissues (of a biomaterial) that can be administered directly to the treated site (page 5, lines 20-26). Furthermore, Pressato et al. disclose that their benzyl ester of hyaluronic acid can be 75-100% esterified (see claim 1). In addition, Pressato et al. disclose that biodegradable and non-biodegradable materials such as polymers in their composition.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Willoughby et al. and Pressato et al., to have used the method of Willoughby et al. to treat tumors by inhibiting angiogenesis with a composition (e.g., a biomaterial) comprising a benzyl ester of hyaluronic acid, since Willoughby et al. suggests that esters of hyaluronic acid can be used by application to the tumor site and Pressato et al. disclose that benzyl ester of hyaluronic acid can be prepared in the form of gels, membranes, woven tissues or meshes and nonwoven tissues (of a biomaterial) that can be administered directly to a treated site.

One having ordinary skill in the art would have been motivated in view of Willoughby et al. and Pressato et al., to have used the method of Willoughby et al. to treat tumors by inhibiting angiogenesis with a composition (e.g., a biomaterial) comprising a benzyl ester of hyaluronic acid, since Willoughby et al. suggests that esters of hyaluronic acid can be used by application to the tumor site and Pressato et al. disclose that benzyl ester of hyaluronic acid can be prepared in the form of gels, membranes, woven tissues or meshes and nonwoven tissues (of a biomaterial) that can be administered directly to a treated site. It should be noted that it is obvious to further include or use pharmaceutically active substance such as antitumor or cancer drugs to treat said tumors. It should also be noted that the formation of granulation tissue is considered an inherent effect of the ester of hyaluronic acid which results due to the inhibition or regression of angiogenesis.

Claim 31 is drawn to a method for the treatment and care of primary and secondary tumors by inhibiting angiogenesis which comprises applying at the tumor site a biomaterial consisting essentially of a benzyl ester of hyaluronic acid wherein said hyaluronic acid is at least 85% benzyl esterified, wherein said biomaterial inhibits angiogenic processes related to vascularization and wherein said biomaterial is in the form of at least one member selected from the group consisting of a non-woven felt, sponge, microsphere, film and membrane. Claims 32-35, 37-38 are drawn to said method wherein said hyaluronic acid is benzyl esterified at specific % and specific form of application to tumor site and wherein the vascularisation and specific tumor cell invasion is specifically limited..

Willoughby et al. disclose the use of hyaluronic acid, including hyaluronic acid esters for the treatment of tumors by inhibiting or regressing angiogenesis (see claims 48-58; see also claims 24-34). Furthermore, Willoughby et al. disclose that their invention provides a process for the inhibition, control and/or regression of angiogenesis, (for example the inhibition of blood vessel growth to a malignant tumour, cutting off blood vessel growth or development, in to a malignant tumour) in a mammal (for example a human), the process comprising the steps of administering an effective dosage amount of a pharmaceutical composition for the inhibition, control and/or regression of angiogenesis to a site on/in the mammal in need of inhibition, control and/or regression ….. (see page 7, lines 6-32; see also page 6, lines 13-21).

The difference between applicant's claimed method and the method disclosed by Willoughby et al. is that Willoughby et al. do not recite the use of a specific ester (i.e., benzyl ester) of hyaluronic acid but teach that esters of hyaluronic acid can be used.

Pressato et al. disclose a biomaterial comprised of benzyl ester of hyaluronic acid in the form of gels, membranes, woven tissues or meshes and nonwoven tissues that can be used to prevent surgical adhesion (page 5, lines 20-26). This suggests that benzyl ester of hyaluronic acid can be in the form of gels, membranes, woven tissues or meshes and nonwoven tissues (of a biomaterial) that can be administered directly to the treated site (page 5, lines 20-26). Furthermore, Pressato et al. disclose that their benzyl ester of hyaluronic acid can be 75-100% esterified (see claim 1). In addition, Pressato et al. disclose that biodegradable and non-biodegradable materials such as polymers in their composition.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Willoughby et al. and Pressato et al., to have used the method of Willoughby et al. to treat tumors by inhibiting angiogenesis with a composition (e.g., a biomaterial) consisting essentially of a benzyl ester of hyaluronic acid, since Willoughby et al. suggests that esters of hyaluronic acid can be used by application to the tumor site and Pressato et al. disclose that benzyl ester of hyaluronic acid can be prepared in the form of gels, membranes, woven tissues or meshes and nonwoven tissues (of a biomaterial) that can be administered directly to a treated site.

One having ordinary skill in the art would have been motivated in view of Willoughby et al. and Pressato et al., to have used the method of Willoughby et al. to treat tumors by inhibiting angiogenesis with a composition (e.g., a biomaterial) consisting essentially of a benzyl ester of hyaluronic acid, since Willoughby et al. suggests that esters of hyaluronic acid can be used by application to the tumor site and Pressato et al. disclose that benzyl ester of hyaluronic acid can be prepared in the form of gels, membranes, woven tissues or meshes and nonwoven tissues (of a biomaterial) that can be administered directly to a treated site. It should be noted that it is obvious to further include or use pharmaceutically active substance such as antitumor or cancer drugs to treat said tumors. It should also be noted that the formation of granulation tissue is considered an inherent effect of the ester of hyaluronic acid which results due to the inhibition or regression of angiogenesis.

Response to Arguments

Applicant's arguments with respect to claims 18, 22-27 and 30-38 have been considered but are not found convincing.

The Applicant argues that Willoughby et al. actually only teaches that a combination of hyaluronic acid with a NSAID can be effective for controlling and/or regressing angiogenesis. On the contrary however, Willoughby et al. disclose that the hyaluronic acid is therapeutically effective substance or component for inhibiting or treating angiogenesis (see abstract). In addition, Willoughby et al. disclose or claims that the hyaluronic acid is can be used alone for inhibiting or treating angiogenesis (see claims 41 and 48). It should be noted that a reference is not limited to its working examples, but must be evaluated for what it teaches those of ordinary skill in the art. In re Boe, 355 F.2d 961, 148 U.S.P.Q. 507 (C.C.P.A. 1966). In re Chapman, 357 F.2d 418, 148 U.S.P.Q. 711 (C.C.P.A. 1966).

The Applicant argues that claim 18 has been amended to recite that the biomaterial that inhibits angiogenic processes related to vasularisation "by granulation tissue forming over the biomaterial". This is contrary to Willoughby et al wherein the experimentally induced granulation tissue is actually reduced as a consequence of the effects of the treatment. However, Willoughby et al. does not teach that the inhibition of angiogenesis causes the reduction of granulation tissue nor granulation tissue formation. But, Willoughby et al. disclose the use of hyaluronic acid, including hyaluronic acid esters for the treatment of tumors by inhibiting or regressing angiogenesis (see claims 48-58; see also claims 24-34). Furthermore, Willoughby et al. disclose that their invention provides a process for the inhibition, control and/or regression of angiogenesis, (for example the inhibition of blood vessel growth to a malignant tumour, cutting off blood vessel growth or development, in to a malignant tumour) in a mammal (for example a human), the process comprising the steps of administering an effective dosage amount of

a pharmaceutical composition for the inhibition, control and/or regression of angiogenesis to a site on/in the mammal in need of inhibition, control and/or regression ….. (see page 7, lines 6-32; see also page 6, lines 13-21). Also, it should be noted that the formation of granulation tissue is considered an inherent effect of the ester of hyaluronic acid which results due to the inhibition or regression of angiogenesis.

The Applicant argues that the Examiner's selection of Pressato et al as a secondary reference is based only on the Examiner's desire to find some prior art reference that teaches benzyl esters of hyaluronic acid per se, and not based on the view of one skilled in the art at the time of Applicant's invention. However, as set forth in the above rejection, one having ordinary skill in the art would have been motivated in view of Willoughby et al. and Pressato et al., to have used the method of Willoughby et al. to treat tumors by inhibiting angiogenesis with a composition (e.g., a biomaterial) consisting essentially of a benzyl ester of hyaluronic acid, since Willoughby et al. suggests that esters of hyaluronic acid can be used by application to the tumor site and Pressato et al. disclose that benzyl ester of hyaluronic acid can be prepared in the form of gels, membranes, woven tissues or meshes and nonwoven tissues (of a biomaterial) that can be administered directly to a treated site.

The Applicant argues that Pressato et al. teaches nothing concerning inhibition of angiogenesis or of tumor growth, nor anything regarding granulation tissue. However, Pressato et al. disclose a biomaterial comprised of benzyl ester of hyaluronic acid in the form of gels, membranes, woven tissues or meshes and nonwoven tissues that can be used to prevent surgical adhesion (page 5, lines 20-26). This suggests that benzyl ester of hyaluronic acid can be in the form of gels, membranes, woven tissues or meshes and

nonwoven tissues (of a biomaterial) that can be administered directly to the treated site (page 5, lines 20-26). Furthermore, Pressato et al. disclose that their benzyl ester of hyaluronic acid can be 75-100% esterified (see claim 1). In addition, Pressato et al. disclose that biodegradable and non-biodegradable materials such as polymers in their composition.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
August 12, 2008.

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623